(FILE 'HOME' ENTERED AT 15:47:37 ON 14 MAY 2006)

FILE 'CAPLUS' ENTERED AT 15:47:49 ON 14 MAY 2006

L1	13	S	54143-55-4/PREP
L2	38	S	54143-55-4/PROC
L3	51	S	L1 OR L2
L4	0	S	HALOBENZOIC ACID AND L3
L5	4	S	BENZOIC ACID AND L3
L6	45	S	L3 AND PY<2003
L7	6	S	L6 AND BENZO?
L8	7	S	L7 OR L5

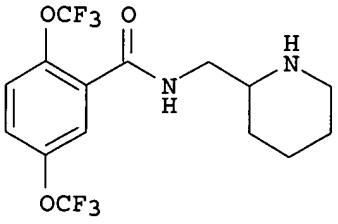
=>

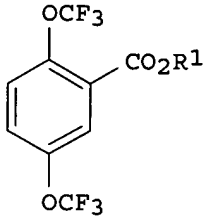
=> d 1-7 ibib abs hitstr

L8 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:238745 CAPLUS
DOCUMENT NUMBER: 142:297883
TITLE: A novel process for preparation of antiarrhythmic flecainide and its intermediates
INVENTOR(S): Wang, Zhi-Xian; Li, Yuanqiang; Guntoori, Bhaskar Reddy
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005059825	A1	20050317	US 2003-663836	20030917
PRIORITY APPLN. INFO.:			US 2003-663836	20030917

OTHER SOURCE(S): CASREACT 142:297883; MARPAT 142:297883
GI

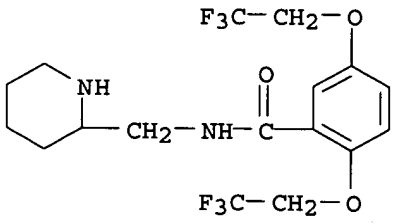

I


II

AB The invention relates to a process for preparation of antiarrhythmic flecainide (I) and its intermediates of formula II (R1 is H, alkali metal, or alkyl). Flecainide (I) was prepared via amidation of II (R1 = Me) by 2-(aminomethyl)piperidine with a yield of 85%. This new process is an inexpensive and efficient process for manufacture of flecainide and its intermediates.

IT **54143-55-4P**, Flecainide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP (Preparation)**
(novel process for preparation of antiarrhythmic flecainide and its intermediates)

RN 54143-55-4 CAPLUS
CN Benzamide, N-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)- (9CI) (CA INDEX NAME)



L8 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:658065 CAPLUS
DOCUMENT NUMBER: 137:201232
TITLE: Flecainide synthesis
INVENTOR(S): McDaniel, William C.; Radhakrishnan, Jayaramaiyer; Janicki, Slawomir J.
PATENT ASSIGNEE(S): Narchem Corporation, USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

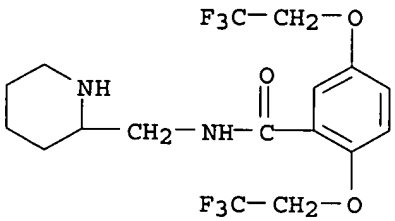
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002066413	A1	20020829	WO 2002-US5390		20020220 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004220409	A1	20041104	US 2003-468628		20030820
PRIORITY APPLN. INFO.:			US 2001-270048P	P	20010220
			US 2001-271788P	P	20010227
			WO 2002-US5390	W	20020220

OTHER SOURCE(S): CASREACT 137:201232; MARPAT 137:201232

AB An improved, highly efficient method for the preparation of flecainide acetate or other pharmaceutically acceptable salts of flecainide involves preparing the staring material 1,4-bis(2,2,2-trifluoroethoxy)benzene in high yields by reacting 4-fluoro-1-bromobenzene with F3CCH2OH in the presence of a base and a copper-containing catalyst.

IT **54143-55-4P**, Flecainide
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(flecainide synthesis)

RN 54143-55-4 CAPLUS
CN Benzamide, N-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:861473 CAPLUS
DOCUMENT NUMBER: 134:32972
TITLE: Porous drug matrixes containing polymers and sugars and methods of their manufacture
INVENTOR(S): Straub, Julie; Bernstein, Howard; Chickering, Donald

E., III; Khatak, Sarwat; Randall, Greg
PATENT ASSIGNEE(S): Acusphere, Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000072827	A2	20001207	WO 2000-US14578	20000525 <--
WO 2000072827	A3	20010125		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6395300	B1	20020528	US 1999-433486	19991104 <--
CA 2371836	AA	20001207	CA 2000-2371836	20000525 <--
CA 2371836	C	20060131		
EP 1180020	A2	20020220	EP 2000-939365	20000525 <--
EP 1180020	B1	20051214		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY				
BR 2000010984	A	20020430	BR 2000-10984	20000525 <--
JP 2003500438	T2	20030107	JP 2000-620939	20000525
NZ 516083	A	20030829	NZ 2000-516083	20000525
AU 768022	B2	20031127	AU 2000-54459	20000525
AT 312601	E	20051215	AT 2000-939365	20000525
EP 1642572	A1	20060405	EP 2005-27194	20000525
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
ES 2250141	T3	20060416	ES 2000-939365	20000525
US 2002041896	A1	20020411	US 2001-798824	20010302 <--
US 6610317	B2	20030826		
NO 2001005753	A	20020128	NO 2001-5753	20011126 <--
ZA 2001010347	A	20030730	ZA 2001-10347	20011218

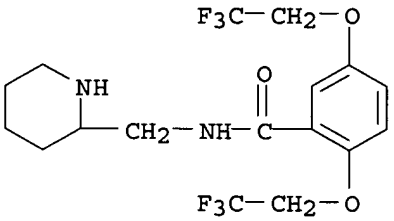
PRIORITY APPLN. INFO.:		
US 1999-136323P	P	19990527
US 1999-158659P	P	19991008
US 1999-433486	A	19991104
US 2000-186310P	P	20000302
EP 2000-939365	A3	20000525
WO 2000-US14578	W	20000525

AB Drugs, especially low aqueous solubility drugs, are provided in a porous matrix form, preferably microparticles, which enhances dissoln. of the drug in aqueous media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aqueous solubility, in a volatile solvent to form a drug solution, (ii) combining at least one pore forming agent with the drug solution to form an emulsion, suspension, or second solns., and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second solution to yield the porous matrix of drug. The pore forming agent can be either a volatile liquid that is immiscible with the drug solvent or a volatile solid compound, preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are

reconstituted with an aqueous medium and administered parenterally, or processed using standard techniques into tablets or capsules for oral administration. Paclitaxel or docetaxel can be provided in a porous matrix form, which allows the drug to be formulated without solubilizing agents and administered as a bolus. For example, a nifedipine-loaded organic solution was prepared by dissolving 9.09 g of PEG 3350, 2.27 g of nifedipine, and 0.009 g of lecithin in 182 mL of methylene chloride. An aqueous solution was prepared by dissolving 3.27 g of NH4HCO3 and 0.91 g of PEG 3350 in 1.82 mL of water. The aqueous and organic solns. were homogenized and resulting emulsion was spray dried. A suspension of the porous nifedipine drug matrix was prepared in 5% dextrose solution at a concentration of 2.5 mg/mL. A bolus injection of the suspension was tolerated when administrated to dogs.

IT **54143-55-4**, Flecainide
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); **PROC (Process)**; USES (Uses)
(preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

RN 54143-55-4 CAPLUS
CN Benzamide, N-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)- (9CI) (CA INDEX NAME)



L8 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:40090 CAPLUS
DOCUMENT NUMBER: 132:103844
TITLE: Extractableness of relevant toxicological compounds with 1-chlorbutane
AUTHOR(S): Demme, U.; Becker, J.; Bussemas, H.; Daldrup, Th.; Erdmann, F.; Erkens, M.; Iten, P. X.; Magerl, H.; Von Meyer, L.; Teske, J.; Weinmann, W.; Weller, J. P.
CORPORATE SOURCE: Institut fur Rechtsmedizin Friedrich-Schiller-Universitat, Jena, D-07740, Germany
SOURCE: GTFCh-Symposium: Nachweis Berauschender Mittel im Strassenverkehr -- Forensische Aspekte der Toxischen Praeparation von Lebensmitteln, Beitraegezum Symposium der Gesellschaft fuer Toxikologische und Forensische Chemie, 11th, Mosbach, Germany, Apr. 22-24, 1999 (**1999**), 213-218. Editor(s): Pragst, Fritz; Aderjan, Rolf. Verlag Dr. Dieter Helm: Heppenheim, Germany.
CODEN: 68NJAK
DOCUMENT TYPE: Conference
LANGUAGE: German

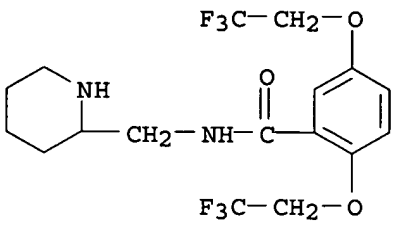
AB Extractability of 160 active components was tested in aqueous solution and blood serum (phosphate-buffer, pH = 9) with 1-chlorobutane in interlab. tests. Extraction yields were determined and partial compared with values from literature.

IT **54143-55-4**, Flecainide

RL: PEP (Physical, engineering or chemical process); **PROC (Process)**
(extractableness of relevant toxicol. compds. from water and blood serum with 1-chlorbutane)

RN 54143-55-4 CAPLUS

CN Benzamide, N-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:64776 CAPLUS

DOCUMENT NUMBER: 130:124996

TITLE: Process and a novel intermediate for the preparation of Flecainide

INVENTOR(S): Gutman, Arie L.; Nisnevich, Genady; Shkolnik, Eleonora; Zaltzman, Igor

PATENT ASSIGNEE(S): Finetech Ltd., Israel

SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

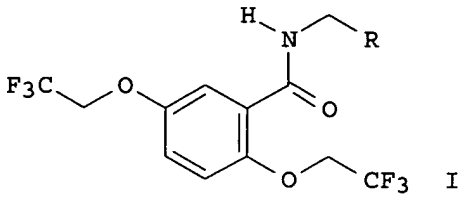
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902498	A1	19990121	WO 1998-IL315	19980707 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
IL 121288	A1	20001031	IL 1997-121288	19970711 <--
AU 9881265	A1	19990208	AU 1998-81265	19980707 <--
EP 996616	A1	20000503	EP 1998-931000	19980707 <--
EP 996616	B1	20040512		
R: ES, FR, IT				
US 6316627	B1	20011113	US 1999-422931	19991021 <--
US 6538138	B1	20030325	US 2000-462418	20000403
US 2002133013	A1	20020919	US 2001-911366	20010723 <--
US 6593486	B2	20030715		

PRIORITY APPLN. INFO.:

IL 1997-121288	A	19970711
IL 1997-120715	A	19970421
WO 1998-IL187	A2	19980420
WO 1998-IL315	W	19980707
US 1999-422931	A1	19991021

OTHER SOURCE(S): CASREACT 130:124996; MARPAT 130:124996

GI



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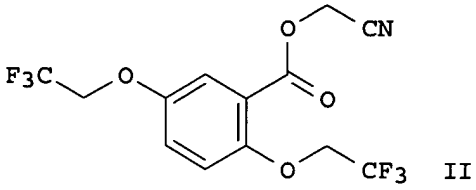


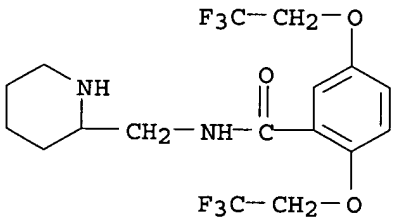
II

AB The title compds. [I; R = 2-piperidyl, 2-pyridyl] and their pharmaceutically acceptable salts, were prepared by a) reacting 2,5-bis(2,2,2,-trifluoroethoxy)**benzoic acid** or its salt with a haloacetonitrile XCH2CN (wherein X = Cl, Br, I) if necessary in the presence of an inorg. or organic base, b) reacting the cyanomethyl ester II with an amine RCH2NH2; c) converting the compound I to its pharmaceutically acceptable salt.

IT **54143-55-4P**, Flecainide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP (Preparation)**
(process and a novel intermediate for the preparation of Flecainide)

RN 54143-55-4 CAPLUS

CN Benzamide, N-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:293427 CAPLUS
DOCUMENT NUMBER: 129:8597
TITLE: Embedding and encapsulation of controlled release particles
INVENTOR(S): Van Lengerich, Bernhard H.
PATENT ASSIGNEE(S): Van Lengerich, Bernhard H., USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9818610	A1	19980507	WO 1997-US18984	19971027 <--
W: AU, CA, JP, NO, PL, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2269806	AA	19980507	CA 1997-2269806	19971027 <--
CA 2269806	C	20060124		

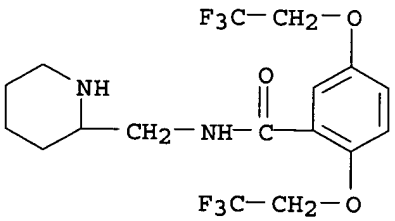
AU 9749915	A1	19980522	AU 1997-49915	19971027 <--
AU 744156	B2	20020214		
EP 935523	A1	19990818	EP 1997-912825	19971027 <--
EP 935523	B1	20040929		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002511777	T2	20020416	JP 1998-520558	19971027 <--
EP 1342548	A1	20030910	EP 2003-10031	19971027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 277739	E	20041015	AT 1997-912825	19971027
NO 9902036	A	19990428	NO 1999-2036	19990428 <--
PRIORITY APPLN. INFO.:			US 1996-29038P	P 19961028
			US 1997-52717P	P 19970716
			EP 1997-912825	A3 19971027
			WO 1997-US18984	W 19971027

AB Controlled release, discrete, solid particles which contain an encapsulated and/or embedded component such as a heat sensitive or readily oxidizable pharmaceutically, biol., or nutritionally active component are continuously produced without substantial destruction of the matrix material or encapsulant. A release-rate controlling component is incorporated into the matrix to control the rate of release of the encapsulant from the particles. The addnl. component may be a hydrophobic component or a high water binding capacity component for extending the release time. The plasticizable matrix material, such as starch, is admixed with at least one plasticizer, such as water, and at least one release-rate controlling component under low shear mixing conditions to plasticize the plasticizable material without substantially destroying the at least one plasticizable material and to obtain a substantially homogeneous plasticized mass. The plasticizer content is substantially reduced and the temperature of the plasticized mass is substantially reduced prior to admixing the plasticized mass with the encapsulant to avoid substantial destruction of the encapsulant and to obtain a formable, extrudable mixture The mixture is extruded though a die without substantial or essentially no expansion and cut into discrete, relatively dense particles. Release properties may also be controlled by precoating the encapsulant and/or coating the extruded particles with a film-forming component. An example of encapsulation of acetylcysteine is given using starch, polyethylene, glycerol monostearate, and vegetable oil.

IT **54143-55-4**, Flecainide
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); **PROC (Process)**; USES (Uses)
(embedding and encapsulation of controlled release particles)

RN 54143-55-4 CAPLUS

CN Benzamide, N-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:122069 CAPLUS
DOCUMENT NUMBER: 114:122069

TITLE: Preparation of 2,5-bis(2,2,2-trifluoroethoxy-N-(2-piperidinylmethyl)benzamide acetate

INVENTOR(S): Rubio Zurita, Pelayo; Cirera Dotti, Xavier; Irurre Perez, Jose

PATENT ASSIGNEE(S): Laboratorios Rubio S. A., Spain

SOURCE: Span., 7 pp.
CODEN: SPXXAD

DOCUMENT TYPE: Patent

LANGUAGE: Spanish

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2007802	A6	19890701	ES 1988-830	19880318 <--
PRIORITY APPLN. INFO.:			ES 1988-830	19880318

OTHER SOURCE(S): MARPAT 114:122069

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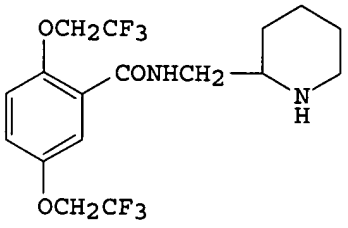

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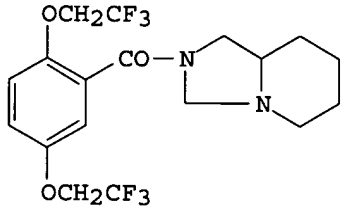

IV

AB The title compound (I.HOAc) is prepared by reaction of an activated derivative of 2,5-bis(2,2,2-trifluoroethoxy)**benzoic acid** (II) with 2-azaindolizidine (III) to give the heterocyclic amide IV as the HCl salt, which is selectively hydrolyzed to I followed by salification with glacial HOAc. Thus, II was treated with SOCl2 at room temperature to give the acid chloride, which reacted with distilled III in CH2Cl2 to give 97% IV.HCl. The latter was hydrolyzed with aqueous HCl in EtOH to give 81% I, which was treated with HOAc in Me2CHOH.

IT **54143-55-4P**, Flecainide
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of, from bis(trifluoroethoxy)**benzoic acid** and azaindolazidine)

RN 54143-55-4 CAPLUS

CN Benzamide, N-(2-piperidinylmethyl)-2,5-bis(2,2,2-trifluoroethoxy)- (9CI) (CA INDEX NAME)